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(51) International Patent Classification ⁵ : C12N 15/70, 15/13, 15/62 C07K 15/28		A3	(11) International Publication Number: WO 93/22332 (43) International Publication Date: 11 November 1993 (11.11.93)
(21) International Application Number: PCT/US93/03895 (22) International Filing Date: 26 April 1993 (26.04.93) (30) Priority data: 07/873,930 24 April 1992 (24.04.92) US 07/963,333 19 October 1992 (19.10.92) US (60) Parent Applications or Grants (63) Related by Continuation US 07/963,333 (CIP) Filed on 19 October 1992 (19.10.92) US 07/873,930 (CIP) Filed on 24 April 1992 (24.04.92) (71) Applicant (for all designated States except US): BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM [US/US]; 201 West 7th Street, Austin, TX 78701 (US).		(72) Inventors; and (75) Inventors/Applicants (for US only): WARD, Elizabeth, Sally [GB/US]; 12856 Noel Road, Apt. 2099, Dallas, TX 75230 (US). KIM, Jin-Kyoo [KR/US]; 4152 W. Pioneer Street, Apt. 1008, Irving, TX 75061 (US). (74) Agent: KITCHELL, Barbara, S.; Arnold, White & Durkee, P.O. Box 4433, Houston, TX 77210 (US). (81) Designated States: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments. (88) Date of publication of the international search report: 17 February 1994 (17.02.94)	
(54) Title: RECOMBINANT PRODUCTION OF IMMUNOGLOBULIN-LIKE DOMAINS IN PROKARYOTIC CELLS			
(57) Abstract			
<p>Disclosed are recombinant vectors encoding immunoglobulin-like domains and portions thereof, such as T-cell variable domains, antidoby Fc-hinge fragments, subfragments and mutant domains with reduced biological half lives. Methods of producing large quantities of such domains, heterodimers, and fusion proteins following expression and secretion by prokaryotic host cells are also reported. Described are single chain T-cell receptors, which are folded into β-pleated sheet structures similar to those of immunoglobulin variable domains; antibody Fc and Fc-hinge domains, which have the same <i>in vivo</i> stability as intact antibodies; and domains engineered to have reduced <i>in vivo</i> half lives. These DNA constructs and protein domains will be useful as templates for <i>in vitro</i> mutagenesis and high resolution structural studies; for immunization and vaccination; and for the production of recombinant antibodies or chimaeric proteins with increased or decreased stability and longevity for therapeutic and diagnostic uses.</p>			

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 93/03895

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 C12N15/70 C12N15/13 C12N15/62 C07K15/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 5 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SCANDINAVIAN JOURNAL OF IMMUNOLOGY vol. 34, no. 2, August 1991 pages 215 - 220 E.S. WARD 'Expression and secretion of T-cell receptor V-alpha and V-beta domains using Escherichia coli as a host' see abstract see page 216, left column, paragraph 2 see page 216, right column, last paragraph - page 218, right column, paragraph 2 --- -/--	1-11, 23, 25-31, 40, 41

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

23 November 1993

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INTERNATIONAL SEARCH REPORT

Inter. nal Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>NATURE vol. 341, no. 6242, 12 October 1989, LONDON GB pages 544 - 546 E. SALLY WARD ET AL. 'Binding activities of a repertoire of single immunoglobulin variable domains secreted from Escherichia coli' see abstract see page 544, right column, last paragraph - page 545, left column, paragraph 3 ---</p>	<p>1-4,22, 25,26, 28-30,40</p>
X	<p>EP,A,0 368 684 (MEDICAL RESEARCH COUNCIL) 16 May 1990 see column 1, line 1 - line 10 see column 4, line 35 - column 5, line 32 see column 15, line 12 - line 25 see column 24, line 49 - column 26, line 30 ---</p>	<p>1,3,4,8, 9,23,25, 26,28-30</p>
X	<p>WO,A,91 08298 (GENENTECH, INC.) 13 June 1991 see page 1, line 3 - line 6 see page 4, line 29 - page 5, line 2 see page 5, line 18 - line 23 see page 7, line 26 - line 36 see page 10, line 29 - line 38 ---</p>	<p>44,45, 64-68</p>
X	<p>PATENT ABSTRACTS OF JAPAN vol. 13, no. 101 (C-574)(3449) 9 March 1989 & JP,A,63 276 496 (KYOWA HAKKO KOGYO CO LTD) 14 November 1988 see abstract ---</p>	<p>1,3-5, 12,23, 25,26, 28-30, 40,48</p>
X	<p>WO,A,92 01787 (CAMBRIDGE ANTIBODY TECHNOLOGY LIMITED) 6 February 1992 see page 5, line 21 - line 28 see page 6, line 8 - page 8, line 21 ---</p>	<p>64,65, 67,68</p>
P,X	<p>IMMUNOLOGY LETTERS vol. 33, no. 1, June 1992 pages 53 - 60 MARK SUTER ET AL. 'Rabbit single domain antibodies specific to protein C expressed in prokaryotes' see page 53, right column, paragraph 2 - page 54, left column, paragraph 3 see page 54, right column, last paragraph - page 55, left column, paragraph 2 -----</p>	<p>1,3,4, 25-30, 40,44,45</p>

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INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 93/03895

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